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The refractive development of untreated eyes of rhesus monkeys varies according to the treatment received by their fellow eyes

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Abstract

To determine the extent to which the visual experience of one eye may influence the refractive development of its fellow eye, we analyzed the data of untreated (UT) eyes of monkeys that received different types of unilateral pattern deprivation. Subjects were 15 juvenile rhesus monkeys, with five monkeys in each of three treatment groups: aphakic eyes with optical correction (AC), aphakic eyes with no correction (ANC), and eyes that were occluded with an opaque contact lens (OC). Under general anaesthesia, refractive error (D) was determined by cycloplegic retinoscopy and axial length (mm) was determined with A-scan ultrasonography. For measurements of refractive error of the UT eyes, there was a significant main effect of groups according to the treatment of the fellow eyes, $F(2, 12) = 6.6$. While UT eyes paired with AC fellow eyes (mean = +4.2 D) were significantly more hyperopic than the eyes of age-matched normal monkeys (mean = +2.4 D), $t(25), = 2.5$, UT eyes paired with OC fellow eyes (mean = −0.5 D) were significantly more myopic than the eyes of normal monkeys, $t(25) = -9$. UT eyes paired with ANC fellow eyes (mean = +1.9 D) were not significantly different from normal eyes. For measurements of axial length there was also a significant main effect of groups, $F(2, 12) = 6.9$. While UT eyes paired with AC fellow eyes (mean = 16.9 mm) were significantly shorter than the eyes of age-matched normal monkeys (mean = 17.5 mm), $t(25) = 2.3$, UT eyes paired with OC fellow eyes (mean = 18.1 mm) were significantly longer than the eyes of normal monkeys, $t(25) = 2.3$. UT eyes paired with ANC fellow eyes (mean = 17.5 mm) were not significantly different from the eyes of normal monkeys. The measurements of axial length and of refractive error of the UT eyes were also significantly correlated with one another, probably indicating that the differences in refractive error were due to differences in axial length, $r = -0.8$. The present data reveal that despite normal visual experience, UT eyes can have their refractive development altered, systematically, simply as a function of the type of pattern deprivation received by their fellow eyes. These data add to the growing evidence that there is an interocular mechanism that is active during emmetropization. As a consequence, future models of eye growth will need to consider both: (1) the direct influence of visual input on the growing eye; as well as (2) the indirect influence coming from the fellow eye.

Keywords: Aphakia; Axial length; Emmetropization; Refractive error; Visual deprivation

1. Introduction

In most vertebrate species the neonatal eye is too short in relation to the focusing power of its optics. As a result, in the absence of accommodation, neonates have a hyperopic refractive error such that images of distant targets are focused beyond the photoreceptor layer of the retina. At birth, refractive error, and two of its primary components, the curvature of the cornea and the axial length of the eye, are normally distributed and only weakly correlated in humans (Sorsby, 1979; Young & Leary, 1991) and rhesus monkeys (Bradley, Fernandes, Lynn, Tigges & Boothe, 1999a). The process of normal refractive development, or emmetropization, involves the coordination of the maturation of the refractive components of the eye with the axial elongation of the globe. The remarkable precision with which the length of the eye is matched to the power of its optics, as occurs in the majority of adults, suggests that

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genetic and experiential factors work in concert to achieve emmetropia.

The landmark studies of Wiesel and Raviola (1977) and Raviola and Wiesel (1985), which found that visual deprivation can disrupt emmetropization, touched off the extensive use of animal models to determine the factors that influence both normal and abnormal eye growth and refractive development (see Bock & Widdows, 1990 for a review). Early studies documented that unilateral deprivation of patterned vision, using lid-suture or occlusion, induced excessive axial elongation and myopia in the treated eyes compared to their untreated fellow eyes (monkey: von Noorden & Crawford, 1978; Green & Guyton, 1986; Smith, Harwerth, Crawford & von Noorden, 1987; Wilson, Fernandes, Chandler, Tigges, Boothe & Gammon, 1987; Fernandes, 1994; chick: Wallman, Adams & Trachtman, 1981; Hodos & Kuenzel, 1984; Wallman, Turkel & Trachtman, 1987; Irving, Sivak & Callender, 1992; tree shrew: Marsh-Tootle & Norton, 1989; marmoset: Troilo & Judge, 1993). More recently, accumulating evidence indicates that the relationship between visual experience and refractive development is not simply a matter of whether or not patterned input is available, but also, and perhaps more importantly, related to other qualities (e.g. sign and magnitude of defocus) of the visual input.

Numerous studies have shown that the eyes of chicks become either myopic or hyperopic according to the type of defocus imposed by external lenses. For example, Schaeffel, Glasser and Howland (1988) showed that the eyes of chicks compensated for the hyperopic defocus from negative power lenses by growing too long and becoming myopic; concurrent myopic defocus of the fellow eyes, using positive power lenses, produced eyes that were too short and hyperopic. The fact that the eyes of chickens can detect the sign (hyperopic or myopic) of the imposed defocus, and adjust the growth of their eyes appropriately in an effort to achieve emmetropia, indicates that the process of emmetropization relies on the clarity of the visual input available to an eye during postnatal development.

As Schaeffel and Howland (1995) have noted, however, there 'are many results from chickens that have not been obtained in monkeys but are essential for the understanding of human myopia'. That is, while there is overwhelming evidence that birds can easily and correctly adjust the refractive development of their eyes in response to either hyperopic or myopic defocus, the evidence that such an ability exists for the eyes of primates remains equivocal (Crewther, Nathan, Kiely, Brennan & Crewther, 1988; Smith, Hung & Harwerth, 1994; Hung, Crawford & Smith 1995). Highly promising, however, is the recent study by Hung, Crawford and Smith (1995), which suggests that when subjected to mild unilateral hyperopic or myopic defocus, the eyes of infant rhesus monkeys may be capable of bi-directional compensatory eye growth. A straightforward interpretation of their results was complicated by several factors, however, two of which are outlined here briefly because they are particularly relevant for the present study.

First, the monkeys viewed (fixated) with the eye that required the least accommodative effort; the monkeys in the unilateral myopic defocus condition used the defocused or treated eye for fixating, whereas the monkeys in the unilateral hyperopic defocus condition used the fellow untreated eye for fixating. Because primates have a consensual accommodative response between the two eyes, when there is an imbalance in the visual input, such as a difference in the effective refractive error, the fixating eye sets the accommodative posture for both eyes (Quick, Newbern & Boothe, 1994; Flitcroft & Morley, 1997); as was observed by Hung, Crawford and Smith (1995). Consequently, regardless of the treatment condition, all of the fixating eyes received focused input, while all of the eyes not used for fixating received hyperopic defocus. Interestingly, Hung, Crawford and Smith (1995) found that most of the non-fixating eyes grew faster than their fellow fixating eyes. One explanation that was offered for these results was that the eyes of primates may not respond to the sign of defocus, but may simply adopt a 'grow to clarity' strategy (Hung, Crawford & Smith 1995).

More importantly for the present report, however, was that unilateral defocus affected the performance of both eyes (Hung, Crawford & Smith, 1995). Whereas two of the three monkeys reared with 3 Diopters (D) of unilateral hyperopic defocus became more myopic in both eyes, two of the three monkeys reared with 3 D of unilateral myopic defocus became more hyperopic in both eyes. Even though these trends suggested that the eyes of primates may compensate for defocus, they indicated strongly that the refractive development of an eye may not only be a function of the type of visual input provided to that eye, but also a function of the visual experience provided to the fellow eye.

While such a phenomenon has been reported in only two studies of chickens (Sivak, Barrie & Weerheim, 1989; Wildsoet & Wallman, 1995), as discussed below, it is probably a general characteristic of primates. Traditionally, theoretical constructs of the connection between visual experience and emmetropization have taken no notice of the relationship between the two eyes in an organism. The paucity of such observations is not surprising if the model is the chicken. Related to the lateral placement of the eyes, chickens have a narrow binocular field of vision (Erlich, 1981), the capability of independent accommodation in the two eyes (Schaeffel, Howland & Farkas, 1986), and nearly total decussation of the optic nerve (Pettigrew, 1978). In species such as monkeys or humans, however, the

visual system is designed primarily for the two eyes to act as one (Boothe & Brown, 1996). The frontal placement of the eyes has led to the yoking of accommodative posture, pupillary responses, and eye movements, all of which contribute to a complex binocular visual system that underlies a cyclopean view of the world. Given this framework, it is not implausible that primates might have developed some mechanism that attempts to regulate eye growth in a manner that would reduce any refractive imbalance between the two eyes (Hung, Crawford & Smith 1995).

Over the past decade we have reared a large number of rhesus monkeys with different types of unilateral and bilateral manipulations of visual input, and reported that the untreated eyes of monkeys reared with unilateral visual deprivation, as a group, are not different from the eyes of monkeys reared with normal bilateral visual experience (Wilson, Fernandes, Chandler, Tigges, Boothe & Gammon, 1987; Tigges, Tigges, Fernandes, Eggers & Gammon, 1990; Fernandes, 1994). However, in a recent report of the effects of some bilateral manipulations, in which one eye of all the monkeys was restricted to the same visual experience across groups, but where the fellow eyes had one of four different manipulations, we found that the refractive development of the similarly treated eyes varied systematically, according to the treatment received by the fellow eyes (Bradley, Fernandes & Boothe, 1997). It might be argued, however, that some aspect of these binocular manipulations, which involved two abnormal eyes, produced this pattern of results. With that in mind, we report here a re-analysis of the axial length data of our untreated fellow eyes; in our earlier reports, the axial length measurements of the untreated eyes were grouped together, but here the untreated fellow eyes were separated according to the type of pattern deprivation received by their treated eyes; which consisted of: (1) a single plane of focused input; (2) no focused input but retinal illumination; or (3) continuous occlusion. In addition, we now present the measurements of refractive error of these monkeys.

The present results show that despite normal visual input during development, when paired with an eye that receives limited or no patterned visual input, the refractive development of untreated eyes can: (1) differ significantly from the eyes of normal monkeys; and (2) varies systematically across treatment groups. To the best of our knowledge, this interocular effect has not been shown previously in studies on the effects of monocular pattern deprivation on eye growth in either primates or chickens. Therefore, at the very least, the present data provide further support for the existence of an interocular mechanism that has an influence on the emmetropization process of eyes that are receiving normal visual input. We discuss the implications of these results in terms of our current understanding of the role of visual input for emmetropization. We conclude that future models concerned with primate emmetropization will need to include at least two classes of factors: direct influences of visual modulation on the growing eye; and indirect influences coming from the fellow eye.

2. Methods

2.1. Subjects

Measurements of refractive error and axial length were obtained from 15 rhesus monkeys reared with unilateral visual deprivation, as well as 11 monkeys reared with normal bilateral visual experience. Table 1 presents the measurements of cycloplegic retinoscopy and axial length which were obtained soon after birth to confirm that no abnormalities were present in the neonatal eyes prior to treatment. Monkeys were then randomly assigned to one of three experimental groups, in which the right eye was designated as the treated eye and the left eye was untreated. Within 1–5 days of birth, ten monkeys underwent a lensectomy of the right eye rendering that eye aphakic. Details of the lensectomies have been described elsewhere (Gammon, Boothe, Chandler, Tigges & Wilson, 1985; Wilson, Fernandes, Chandler, Tigges, Boothe & Gammon, 1987).

2.2. Treatment groups

The first group consisted of five monkeys in which the aphakic eyes were optically corrected (AC) to a 'near point' using extended-wear contact lenses (EWCLs). We fitted these aphakia-corrected (AC) eyes with EWCLs that provided a 3–5 D over-correction, thus giving clear focus for objects at a distance of about arm's length. The second group of five monkeys consisted of those with aphakic eyes that were not given any optical correction (ANC); as a result, they received little patterned input, but retinal illumination. A third group of five monkeys was fitted with opaque occluders (OC) on the right eye soon after birth. The occluders consisted of plano EWCLs that were dyed black, and attenuated 99% of light transmission. Details of the custom-fitted EWCLs, which we manufacture specifically for the eyes of monkeys in our Contact Lens Laboratory at Yerkes, have been described elsewhere (Gammon, Boothe, Chandler, Tigges & Wilson, 1985; Fernandes, Tigges, Tigges, Gammon & Chandler, 1988).

Throughout development the optical power of the corrective lenses was adjusted individually for each monkey, on the basis of the most recent cycloplegic retinoscopy. For all monkeys fitted with EWCLs, the

Table 1
Neonatal ophthalmic measurements of the untreated (UT) and the treated eyes of the aphakia-corrected (AC), aphakia-not corrected (ANC), and opaque occlusion (OC) groups; and the ages at the time of the later measurements

Monkey	Treatment		Neonatal pre-treatment measurements				Age at later measurements (weeks)
	Rearing conditions		Refractive error (D)		Axial length (mm)		
	Right	Left	Right	Left	Right	Left	
rnn1	AC	UT	+6.0	+6.0	12.8	12.2	57
rjn1	AC	UT	+4.5	+4.5	13.6	13.5	40
rrn2	AC	UT	+4.0	+4.0	13.0	12.9	43
rnk2	AC	UT	+4.0	+4.0	13.2	13.2	61
roq1	AC	UT	+1.0[a]	+0.5[a]	13.4	13.2	50
							Mean, (±S.D.); 50.2, (±8.9)
rhn1	ANC	UT	+3.0	+3.0	13.2	13.1	48
rom1	ANC	UT	+4.0	+4.0	13.5	13.4	61
rkn1	ANC	UT	+2.0	+2.0	13.4	13.3	40
ruo1	ANC	UT	+6.5	+8.0	12.5	12.2	54
rtm1	ANC	UT	+3.0	+3.0	13.2	13.2	50
							Mean, (±S.D.); 50.6 (±7.7)
rjg2	OC	UT	NA	NA	13.8	13.6	53
rkl3	OC	UT	+4.3	+4.5	13.5	14.1	51
rdh2	OC	UT	NA	NA	13.2	13.2	52
rri2	OC	UT	NA	NA	13.8	13.8	48
rsi2	OC	UT	NA	NA	13.7	13.7	29
							Mean, (±S.D.); 46.6, (±10)
Normals ($n = 11$)							Mean, (±S.D.); 49.0, (±5.4)

[a] Not fully cyclopleged at the time of the pre-treatment measurement.

diameters and base curvatures of the EWCLs were changed throughout the lens rearing period as the eyes grew and the corneas flattened; lenses were fitted under the upper and lower eyelids, covering part of the sclera. Seven days a week, the monkeys were monitored for lens-wear every 2 h, and missing lenses were replaced immediately, and noted in a computerized database. Lens-wear compliance was excellent, generally greater than 95% during the lens rearing period.

2.3. Ophthalmic examinations

Examinations were conducted while the monkeys were under general anaesthesia (acepromazine/ketamine 10/90 mg ratio per ml at 0.1 ml/kg). Monkeys were in the supine position with the head immobilized by a head holder. During the examination the eyelids were held open with a speculum, and the cornea was kept irrigated with regular instillation of sterile saline. Measurements obtained specifically for this study were cycloplegic refraction by retinoscopy (three drops of 1% cyclopentolate and three drops of 2.5% phenylephrine hydrochloride at 5 min intervals, 30–45 min prior to retinoscopy); and axial length by A-scan ultrasonography (Sonomed). Even though measurements of corneal curvature were not available for most of these monkeys, since the UT eyes were not manipulated directly, there is no reason to presume that corneal power would differ systematically across groups. Refractive errors are reported as the spherical equivalent in diopters (D). Axial length measurements are reported in mm and are the mean of ten consecutive ultrasound measurements.

As shown in Table 1, most of the data in the present report were obtained shortly before 1 year-of-age, a time when all of the monkeys were still in lenses. This age period was selected for two reasons: (1) 95% of postnatal refractive development has occurred by this age (Bradley et al., 1999a); and (2) this was an age at which both measurements were available for nearly all subjects; the exception to this was monkey rsi2 of the opaque occlusion (OC) group, for whom both measurements were not available beyond 29 weeks of age. The measurements of refractive error and of axial length of the aphakic eyes from the five monkeys in the AC group have been published previously in abstract form (Bradley, Fernandes & Boothe, 1997), and also appear in a manuscript that examines developmental changes in several groups of AC eyes that were reared with different types of binocular manipulations (Bradley, Fernandes, Tigges & Boothe, 1999b). Measurements of axial length at selected ages have also been published previously for many of the monkeys in the present report (Wilson, Fernandes, Chandler, Tigges, Boothe & Gammon, 1987; Tigges, Tigges, Fernandes, Eggers &

Gammon, 1990; Fernandes, 1994; Iuvone, Tigges, Stone, Lambert & Laties, 1991). All of the experimental procedures and the protocols associated with the care and handling of the monkeys conformed to NIH guidelines for the care and use of laboratory animals. The Yerkes Regional Primate Research Center of Emory University is fully accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC).

3. Results

3.1. Refractive error

Fig. 1 shows the mean ($\pm$S.E.M.) measurements of refractive error of the UT eyes of each of the three groups, as a function of the treatment of their fellow eyes. The two horizontal lines designate the mean ($\pm$S.E.M.) refractive error measurements of eleven age-matched normal monkeys. There was a significant main effect of groups for measurements of refractive error of the UT eyes according to the treatment regiment of the fellow eyes, $F(2, 12) = 6.6$, $P < 0.02$. UT eyes paired with AC eyes (mean = 4.2 D, S.D. = 0.6 D) were significantly more hyperopic than either the eyes of normal monkeys (mean = 2.4 D, S.D. = 0.6D), $t(25) = 2.5$, $P < 0.01$, or UT eyes paired with OC fellow eyes (mean = -0.5, S.D. = 0.7 D), $t(8) = -3.1$, $P < 0.01$. Despite the greater degree of hyperopia for the UT eyes paired with AC eyes, relative to the UT eyes paired with ANC eyes (mean = 1.9 D, S.D. = 1 D), given the high variability in the range of measurements obtained for the former, this difference was not significant, $t(8) = 1.5$, $P > 0.05$. UT eyes paired with ANC eyes were not significantly different from normal eyes, $t(25) = -1.43$, $P = 0.08$. UT eyes paired with OC eyes were significantly more myopic than either UT eyes paired with ANC eyes, $t(8) = -6.15$, $P < 0.01$, or normal eyes, $t(25) = -9.3$, $P < 0.01$.

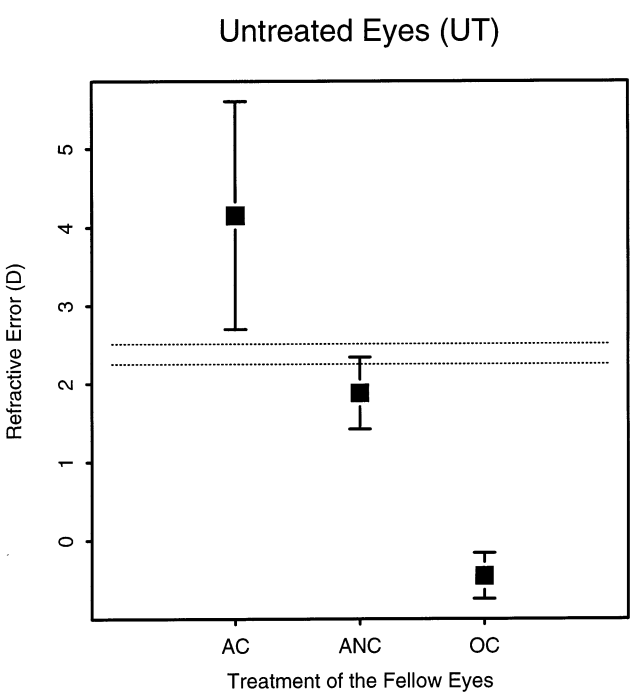

Fig. 1. Mean ($\pm$S.E.M.) refractive error (D) measurements of UT eyes as a function of the treatment received by their fellow treated eyes; fellow eyes were subject to either aphakia with optical correction (AC), aphakia with no optical correction (ANC), or occluded continuously (OC). The two horizontal lines represent $\pm$S.E.M. of age-matched normal monkeys.

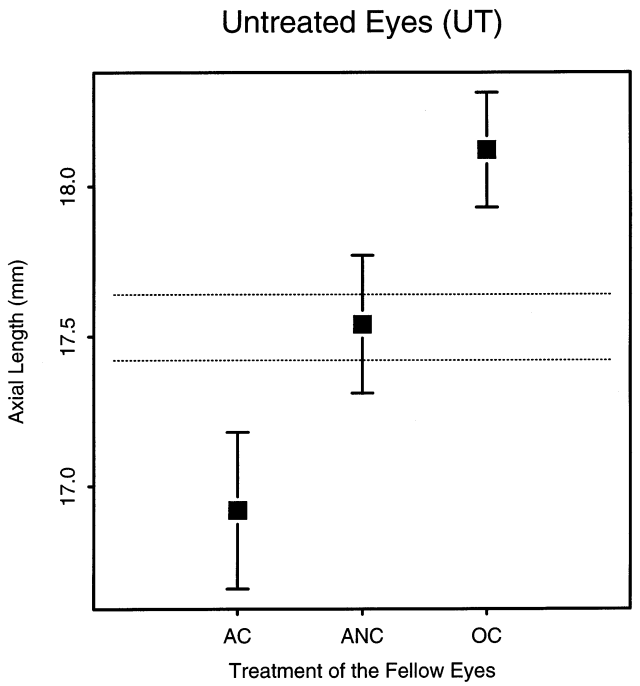

Fig. 2. Mean ($\pm$S.E.M.) axial length (mm) measurements of UT eyes as a function of the treatment received by their fellow treated eyes; fellow eyes were subject to either aphakia with optical correction (AC), aphakia with no optical correction (ANC), or occluded continuously (OC). The two horizontal lines represent the $\pm$S.E.M. of age-matched normal monkeys.

Fig. 2 shows the mean ($\pm$S.E.M.) measurements of axial length of UT eyes as a function of the treatment of their fellow eyes. The two horizontal lines designate the mean ($\pm$S.E.M.) axial length measurements of age-matched normal monkeys. There was a significant main effect of groups according to the treatment of the fellow eyes, $F(2,12) = 6.6$, $P < 0.02$. UT eyes paired with AC eyes (mean = 16.9 mm, S.D. = 0.6 mm) were significantly shorter than either the eyes of normal monkeys (mean = 17.5 mm, S.D. = 0.5 mm), $t(25) = 2.3$, $P < 0.02$ or UT eyes paired with OC eyes (mean = 18.2 mm, S.D. = 0.4 mm), $t(8) = 3.8$, $P < 0.01$. While UT eyes paired with ANC eyes (mean = 17.5 mm, S.D. = 0.5 mm) were not significantly different than

normal eyes, $t(25) = 0.05$, $P > 0.05$, they were nearly significantly longer than UT eyes paired with AC eyes, $t(8) = -1.8$, $P = 0.05$. UT eyes paired with OC eyes were significantly longer than both UT eyes paired with ANC eyes, $t(8) = 1.9$, $P < 0.05$, and normal eyes, $t(25) = 2.14$, $P < 0.02$.

Fig. 3 shows the relationship between the measurements of refractive error and the measurements of axial length for the UT eyes of monkeys in the three treatment groups. Each group is denoted by a different symbol and each of the five monkeys within a group is numbered one through five within a symbol; to assist the reader, the same number represents the data of the same monkey in subsequent graphs. Given the systematic differences between the three groups as shown above, it was not altogether surprising that there was a highly significant correlation between the measurements of refractive error and the measurements of axial length of the UT eyes, Pearson $r = -0.8$, $P < 0.001$. We conclude that the differences in the refractive error measurements of the three groups of UT eyes reflect differences in axial length. Although we did not make separate measurements of the length of the vitreous chamber of the UT eyes, in a normal population, and as shown in numerous studies of visual deprivation in a variety of species, vitreous chamber depth clearly is significantly correlated with the total axial length of the eye, and thus, our expectation is that the differences in the axial length measurements across groups was a function of differences in the length of the posterior segment of the eyes.

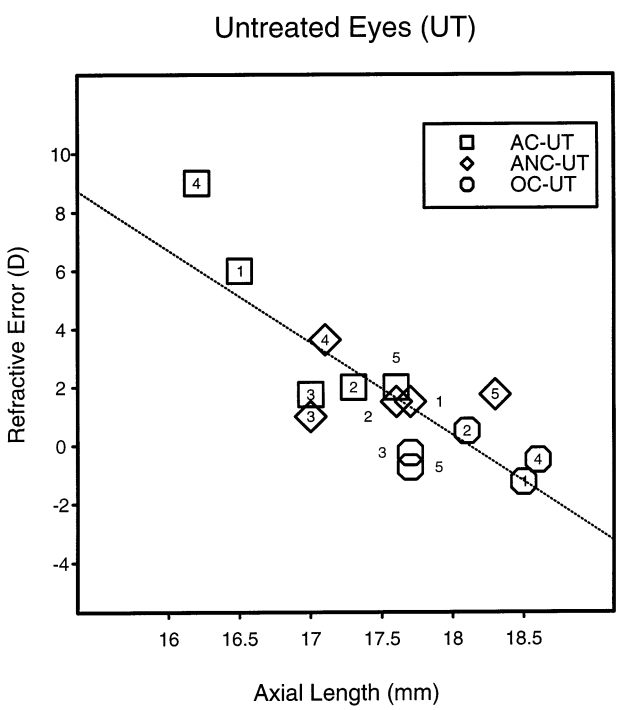

Fig. 3. Scatter plot of the relationship between the measurements of refractive error (D) and the measurements of axial length (mm) of the UT eyes, Pearson $r = -0.8$, $P < 0.01$. Note: Each subject of the AC (aphakia corrected), ANC (aphakia not corrected), and OC (occluded) groups is denoted by a number between 1 and 5, that lies within the symbol assigned to each group; in cases where numbers within the symbols would be obscured because of overlap, the subject's identifying number has been placed adjacent to the appropriate symbol. Each subject's number/symbol identification remains the same in subsequent graphs.

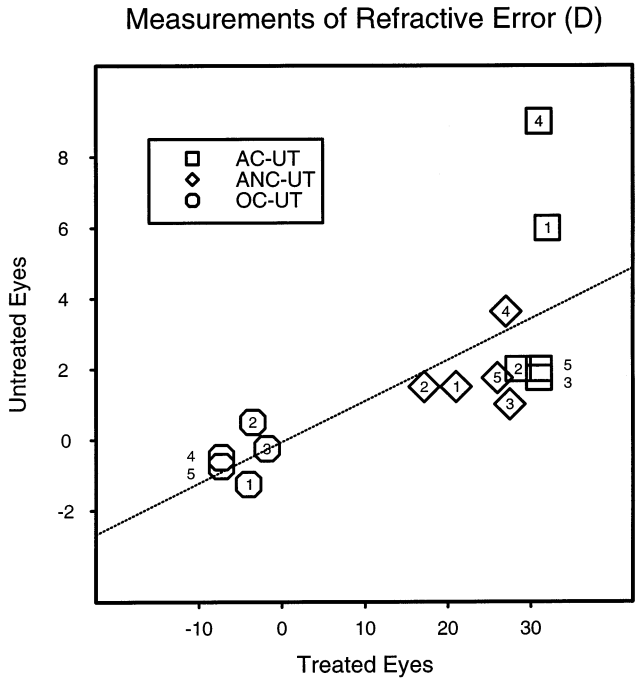

Fig. 4. Scatter plot of the relationship between measurements of refractive error (D) of the UT eyes and the measurements of refractive error (D) of their fellow treated eyes, Pearson $r = 0.7$, $P < 0.01$. An individual's identity is noted as described for Fig. 3.

3.2. Relationship between the two eyes

Figs. 4 and 5 show the relationships between the treated and the UT eyes for measurements of refractive error and measurements of axial length. As shown in Fig. 4, there was a highly significant correlation between the measurements of refractive error for the treated eyes and their respective UT eyes, Pearson $r = 0.7$, $P < 0.01$. OC treated eyes had the highest myopic refraction, and their UT eyes had the greatest myopic shift during refractive development. Likewise, AC eyes, which had the greatest degree of hyperopia, were paired with UT eyes that also had the greatest degree of hyperopia. As shown in Fig. 5, there was also a highly significant correlation for measurements of axial length, Pearson $r = 0.8$, $P < 0.005$. Aphakic eyes were the shortest, and their UT eyes also tended to be short. OC eyes were the longest, and their UT eyes tended to be the longest.

4. Discussion

The current data show that when paired with eyes that received pattern deprivation, untreated fellow eyes can have their refractive status and globe length altered significantly compared to the eyes of normal monkeys. Furthermore, the alterations in eye growth appear to be systematic, varying in relation to the type of visual input provided to their fellow treated eyes. The untreated eye has traditionally served as a normal control, in the sense that its pattern of growth was considered to be independent of whatever manipulation was prescribed for its fellow treated eye. What the present report reveals, however, is that unilateral pattern deprivation can affect the refractive development and axial elongation of both eyes.

Moreover, taken together with the results of Hung, Crawford and Smith (1995), accumulating evidence suggests that this interocular influence may be a general characteristic of emmetropization in primates. Interestingly, a mechanism that attempts to reduce differences between the two eyes is supported further by work concerning emmetropization in normal monkeys (Bradley et al., 1999a). We generated growth curves from several hundred measurements of refractive error, axial length, and corneal curvature. For all three parameters, our analyses revealed that the magnitudes of the interocular differences were relatively high at birth. However, during the most rapid period of postnatal changes in ocular parameters, the differences between the two eyes decreased steadily; this trend is consistent with an active interocular mechanism for emmetropization. Further studies (or re-analyses) will be necessary in order to determine whether in fact this is a general phenomenon across species, or whether it reflects the degree to which an organism's visual system constrains the level of independence between the two eyes, a predominant characteristic of primates (Boothe & Brown, 1996).

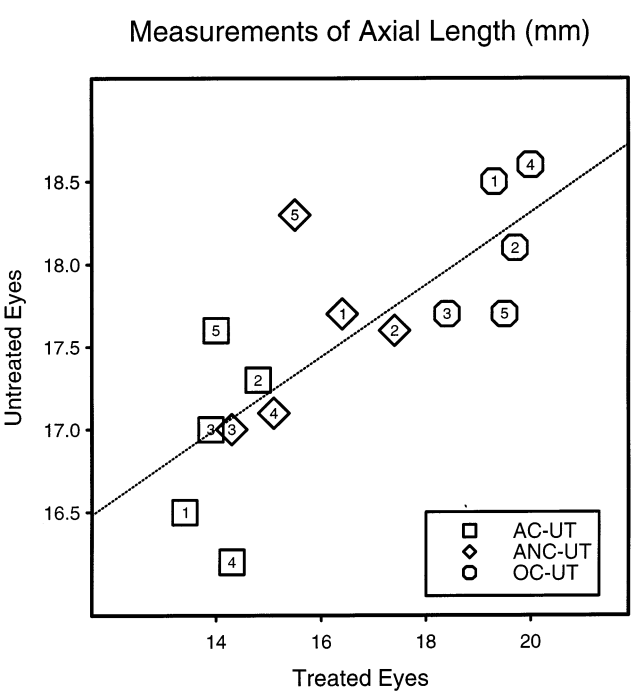

Fig. 5. Scatter plot of the relationship between measurements of axial length (mm) of the UT eyes and the measurements of axial length (mm) of their fellow treated eyes, Pearson $r = 0.76$, $P < 0.01$. An individual's identity is noted as described for Fig. 3.

We do not yet have a unified model to describe the mechanism(s) for these effects. Nevertheless, the present data can be useful in refining our current understanding of the visual regulation of emmetropization. For example, some models have included amblyopia as a mechanism for ametropia associated with defocus (Kiorpes & Wallman, 1995). This mechanism cannot apply to the present results because none of the untreated eyes were amblyopic (Boothe, 1996). Genetic mechanisms have also been proposed on the basis of the finding in chickens that different strains respond differentially to visual deprivation (Troilo, Li, Glasser & Howland, 1995). However, we can rule out that mechanism as well, since all of the monkeys used in the present study were born in the same colony and assigned randomly to treatment groups.

Determining the regulating mechanisms responsible for these interocular effects on the untreated eyes is an extremely important issue. One potential class of mechanisms would involve sensing the refractive status or the rate of axial elongation in both eyes, and then adjusting the rate of growth of each eye to minimize these differences (Hung, Crawford & Smith, 1995). An alternative mechanism would be one where the regulatory mechanisms of one eye are sensitive, and responsive, to the visual experience of the fellow eye. Either scenario would be extremely illuminating for the elucidation of the factors that influence emmetropization, as well as the prevention of disorders such as myopia.

While the present results provide further information regarding the factors that influence postnatal eye growth, they also indicate that this process is perhaps more complex than previously conceived. These results have implications for future studies in the regulation of eye growth. For example, while providing both eyes with identical anomalous visual input might make it possible to examine the direct effects of defocus on an eye's growth, this strategy may tell us nothing about the influence of the indirect growth mechanism. This by no means suggests, however, that unilateral visual deprivation is an inappropriate manipulation for the study of visually-guided refractive development; in fact, in the present report, all of the treated eyes changed in the manner appropriate for their particular deprivation condition. What the present study illuminates, however, is that future studies and models must account for: (1) the direct effect of visual input on an eye, as well as (2)

the indirect influence of the visual experience of the fellow eye. The experimental protocol used in the present study provides a potentially powerful animal model with which to begin the search for this growth-regulating mechanism.

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